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Autobiographical memory in children with Idiopathic Generalised Epilepsy

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ABSTRACT

Autobiographical memory involves the recall of both personal facts (semantic memory) and the re-experiencing of past personal events (episodic memory). The recall of autobiographical episodic details has been associated with a specific network, which involves the prefrontal and medial temporal lobes, in addition to posterior regions of the brain. Seizure activity has been previously shown to disrupt the consolidation of newly-learned information into long-term memory, but it is not yet known whether primary generalised seizures alone are also associated with deficits in the recall of autobiographical memories. Here we examined this recall in children who experience generalised rather than localisation-related seizures: children with Idiopathic Generalised Epilepsy (IGE). In this study, 18 children with IGE and 42 healthy controls of comparable age (6–16 years), sex and socio-economic status were administered the Children's Autobiographical Interview (CAI). Compared with controls, children with IGE recalled significantly fewer episodic details, even when retrieval prompts were provided. In contrast, no group difference was found for the recall of semantic autobiographic details. Within the IGE group, hierarchical regression analyses showed that patient age and earlier age of diagnosis were significantly related to the recall of episodic autobiographical details over different conditions of the CAI, explaining up to 37% of variance. To our knowledge, this study provides the first evidence of autobiographical episodic memory deficits in patients with primary generalised seizures. As no evidence of localisation-related epilepsy is apparent in patients with IGE, our findings suggest that generalised seizures alone, especially when developed at an early age, could compromise memories for personally-experienced events.

1. Introduction

Autobiographical memory is a complex ability that involves mental "time travel" and re-experiencing of personal past events characterised by unique constellations of specific emotional, perceptual, cognitive and temporal details: episodic memory (Levine et al., 2002; Tulving, 2002). Each autobiographical episode is encountered once only and is typically embedded within a context of personal factual information (Levine, 2004): semantic memory. Unlike episodic memory, semantic memory is acquired through repeated exposures and does not involve re-experiencing.

Given that episodic (but not semantic) memories are unique and, once compromised, cannot be completely re-established, episodic memories may be more sensitive to disruption than semantic memories by generalised seizures and/or diffuse pathology underlying generalised seizures. The possibility that generalised seizures could compromise autobiographical episodic memories has received little attention. Research has largely focussed on the involvement of the hippocampus in retrieval of autobiographical event details, which is proposed to be temporally limited and temporally unlimited, according to the classic consolidation theory (CCT, Squire et al., 1984) and multiple trace theory (MTT, Nadel and Moscovitch, 1997), respectively. In one study, however, Lah et al. (2006) compared adult patients with temporal lobe epilepsy (TLE) who experienced generalised seizures (in combination with complex partial seizures) with controls and also patients who experienced complex partial seizures only. Compared with control participants, both TLE patient groups recalled significantly fewer

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autobiographical episodes and less semantic information, although the two patient groups did not differ significantly from each other. However, in this study the temporal lobe seizure focus/abnormality alone could have compromised the recall of autobiographical memories, as temporal lobe pathology has been previously found to disrupt the recollection of episodic and semantic autobiographical details even in patients who do not have a history of seizures, such as those with Alzheimer's disease (Dorrego et al., 1999; Greene and Hodges, 1996; Irish et al., 2011, 2013; Sexton et al., 2010) or semantic dementia (Graham et al., 1997; Irish et al., 2012; Matuszewski et al., 2009; Snowden et al., 1996).

To investigate whether autobiographical memory can potentially be disrupted by generalised seizures alone, patients who experience generalised seizures and no indication of localisation-related epilepsy (i.e., temporal lobe epilepsy), such as patients with Idiopathic Generalised Epilepsy (IGE), would need to be assessed. This form of epilepsy is a common type of epilepsy in childhood, representing approximately 20% of all epilepsies found in children (Jallon and Latour, 2005). Accordingly, the current study examined the autobiographical memory performance in children with IGE.

Epilepsy-related factors such as treatments can also adversely impact memory. One study found that adults with TLE who were on antiepileptic drug polytherapy recalled significantly fewer autobiographical events relative to adults on monotherapy (Lah et al., 2006). However, a recent study found no relationship between polytherapy and recall of autobiographical events in children with TLE (Gascoigne et al., 2013). Moreover, factors such as severity (Helmstaedter, 2002) and longer duration of epilepsy disorder have been found to negatively impact learning and recall of information in both adults (Mameniskiene et al., 2006) and children (Nolan et al., 2004) with epilepsy, but were not related to autobiographical memory in children (Gascoigne et al., 2013) or adults with epilepsy (Lah et al., 2004). Previous studies of children with TLE suggest that memory deficits emerge gradually over the course of development; that children "grow into their memory deficits". For example, a longitudinal study of children with left TLE found that verbal memory deficits only became apparent during their teenage years or young adulthood (Gonzalez et al., 2012) when no such deficits were obvious during childhood (Gonzalez et al., 2007). A large cross-sectional study involving 1000 healthy control subjects (aged 6–80 years) and 1157 patients with TLE (aged 6–68 years) also found that deficits in recall of verbal information after short delays were not evident in children, but became noticeable (relative to healthy controls) during adolescence or young adulthood (Helmstaedter and Elger, 2009).

In addition to epilepsy-related factors, it has been suggested that autobiographical memory deficits in patients with epilepsy may also be secondary to other underlying cognitive deficits, such as impaired short-term recall of newly-learned verbal materials that is evident on standardised memory tests (Lah et al., 2004, 2006). Deficits in the recall of newly-learned information have also been associated with autobiographical memory impairments in non-epilepsy patients, such as those with Korsakoff's syndrome (Mayes et al., 1997; Schmidtke and Vollmer, 1997; Shimamura and Squire, 1986). Interestingly, among patients with TLE, deficits in episodic aspects of autobiographical memory and in short-term recall of newly-learned materials have been found in both adults (Herfurth et al., 2010; Lah et al., 2004, 2006) and children (Gascoigne et al., 2013). However, no significant association has been found between these two memory types. Compared with healthy controls, children with IGE perform significantly more poorly on standardised memory tests (Gascoigne et al., 2012), but whether these deficits compromise autobiographical recall in this patient population is not known.

The aim of this study was to investigate the recall of autobiographical memories in children with IGE. As episodic memories may be more sensitive to disruption from seizure activity than semantic memories, it was hypothesised that children with IGE would exhibit poorer episodic recall than their healthy control peers on a test of autobiographical recall. The impact of other relevant epilepsy variables (such as mono- vs. poly-therapy, epilepsy severity, age at diagnosis and proportion of life with epilepsy) as well as potential associations between performances on the autobiographical memory task, tests of new learning and short-term memory, and chronological age were also examined.

2. Method

2.1. Participants

A total of 18 children with IGE and 42 control children were recruited. All participants were fluent in English and aged between 6 and 16 years at the time of assessment. Participants were excluded for the following reasons: (i) Full Scale Intelligence Quotient (FSIQ) < 80; (ii) presence of a major sensory deficit; (iii) significant neurodevelopmental disorder (e.g. autism, but not learning disability or Attention Deficit Hyperactivity Disorder (ADHD)), or (iv) another neurological disorder.

All IGE participants were recruited from The Children's Hospital at Westmead (CHW), after the ethics committees of both CHW and The University of Sydney approved the study. Initially 24 participants were seen for a neuropsychological assessment. Paediatric neurologists, who were blind to neuropsychological findings, reviewed electroencephalography records, medical history, and clinical imaging data in order to identify participants who met the International League Against Epilepsy criteria for IGE (Commission on Classification and Terminology of the International League Against Epilepsy, 1989). On review, six patients were excluded, as they did not completely meet the diagnostic criteria for IGE. Control participants were free of a history of epilepsy and recruited through the peer networks of the IGE patients and other control participants (snowball recruitment).

Clinical data for the 18 IGE participants are summarised in Table 1. The average age of diagnosis was 6.2 (SD = 3.3) years and mean epilepsy severity rating was 2.3 (SD = 1.7), equivalent to a rating between "A little severe" and "Somewhat severe". One IGE participant had an existing diagnosis of ADHD. All participants were taking anti-epileptic drugs (AEDs) at the time of assessment, 16 were on monotherapy and 2 on polytherapy. Eight different AEDs were represented within the IGE sample, with sodium valproate being the most commonly prescribed drug ($n = 8$). Of the 18 children with IGE, 9 met criteria for the Childhood Absence Epilepsy syndrome, 3 with Febrile Seizures Plus, 2 with Epilepsy with Myoclonic Absences, 1 with Juvenile Absence Epilepsy and 1 with Epilepsy with Generalised Tonic–Clonic Seizures alone. Two patients could not be classified into an IGE syndrome.

2.2. Measures

The standardised clinical neuropsychological instruments used in this study are summarised in Table 2 and standard scores are reported. Average years of parent/guardian education were used as a measure of socioeconomic status (SES).

The Global Assessment of Severity of Epilepsy (GASE; Speechley et al., 2008) scale was used by treating paediatric neurologists to assess the severity of epilepsy in IGE participants. Epilepsy severity ratings [ranging from 1 (not at all severe) to 7 (extremely severe)] were based on the frequency and intensity of seizures, injuries during seizures, number and side effects of antiepileptic drugs,